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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,013	02/06/2001	Terry B. Strom	01948-061001	6231
7590 06/14/2005				
LEE CREWS, Ph.D FISH AND RICHARDSON P.C. 225 Franklin Street Boston, MA 02110-2804			EXAMINER TUNG, JOYCE	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/778,013

Applicant(s)

STROM ET AL.

Examiner

Joyce Tung

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 12-24 and 30-42 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 8-11 and 26-29 is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/29/02, 4/29/02</u> | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1637

### **DETAILED ACTION**

The applicant's response filed 9/17/2004 to the Office action has been entered. Claims 1-42 are pending.

#### ***Election/Restrictions***

1. Applicant's election without traverse of Group I, claims 1-11 and 26-29 in the reply filed on 9/17/2004 is acknowledged.
2. Claims 12-25 and 30-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II-VI, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/17/2004.

#### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1637

4. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strehlau et al. (Proc. Natl. Acad. Sci. USA, 1997, Vol. 94, pg. 695-700) in view of Jeyarajah et al. (Transplantation Proceedings, 1995, Vol. 27(1), pg. 887-889).

Strehlau et al. disclose that during acute renal allograft rejection, intragraft expression of IL-7, IL-10, IL-15 and Fas ligand are increased (See pg. 695, column 1, the Abstract).

Strehlau et al. do not disclose the fluid test sample from a host.

Jeyarajah et al. disclose that the cytokines have been detected in the urine of transplant recipients (See pg. 887, column 1, the abstract).

One of ordinary skill in the art would have been motivated to apply the urine sample to the method of Strehlau et al. for evaluating acute transplant rejection in a host as taught by Jeyarajah et al. because cytokine message was easily detected in the urinary sediment of renal allograft recipients regardless of acute cellular rejection (See pg. 887, column 2, second paragraph). It would have been prima facie obvious to apply urine sample for evaluating acute transplants rejection by determining a magnitude of gene expression in the fluid test sample of at least two genes which are selected from one or more gene clusters, the IL-7/17 cluster, the IL-8 cluster, the IL-10 cluster, and the T cell cluster.

***Allowable Subject Matter***

5. Claims 8-11 and 26-29 are allowable.
6. The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 8-11, no prior art has been found teachings or suggesting a method of determining the cause of delayed graft function in a host comprising determining a magnitude of gene expression of at least one gene of a pro-apoptotic gene cluster in a sample wherein the gene

Art Unit: 1637

of the pro-apoptotic gene cluster is selected from the group consisting of Granzyme B, perforin and Fas ligand and detecting upregulation of the at least one gene which indicates that the delayed graft function is due to immunological causes.

Concerning claims 26-29, no prior art has been found teachings or suggesting a method for evaluating transplant rejection in a host comprising determining a magnitude of gene expression of a cytoprotective gene found in a post transplantation sample and detecting the upregulation of the cytoprotective gene which indicates transplant rejection.

The closest prior art for the allowable subject matter of claims 8-11 is the reference of Suthanthiran (Kidney International Vol.51, Suppl. 58, March, 1997, pp S15-S17). Suthanthiran discloses that the gene expression of Granzyme B and perforin correlates with an acute rejection (See pg. S-15, column 1, third paragraph). Suthanthiran does not disclose that the increased gene expression of Granzyme B and perforin indicates the cause of the delayed graft function.

The closest prior art for the allowable subject matter of claims 26-29 is the reference of Willis et al (Nature Medicine, 1996, Vol.2 (1), pg. 87-90). Willis et al. disclose that heme oxygenase modulates inflammatory response in which elevation of the enzyme results in a striking suppression to a potentiation of the inflammatory response (See pg. 87, column 1, the abstract). Willis et al. do not disclose that the increased gene expression of cytoprotective gene indicates transplant rejection.

### **Summary**

7. Claims 1-7 are rejected.
8. Claims 8-11 and 26-29 are allowable.

Art Unit: 1637

9. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

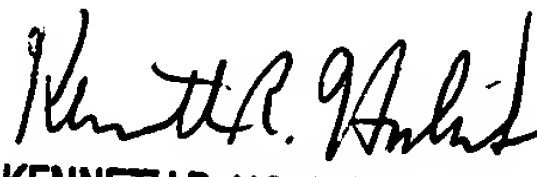
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

May 27, 2005

  
KENNETH R. HORLICK, PH.D.  
PRIMARY EXAMINER

6/13/05